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Moffett Field, California 94035-1000

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13. ABSTRACT *(Maximum 200 words)*

Prevention of secondary brain injuries following head trauma can be accomplished most easily when intracranial pressure (ICP) is monitored. However, current measurement techniques are invasive and thus not practical in the combat environment. The Pulsed Phase Lock Loop (PPLL) device, which was developed and patented by consultants Dr. Yost and Dr. Cantrell, uses a unique, noninvasive ultrasonic phase comparison method to measure slight changes in cranial volume which occur with changes in ICP. Year one studies involved instument improvements and measurement of altered intracranial distance with altered ICP in fresh cadavera. We accomplished our goals for the past year. Our software was improved to facilitate future studies of normal subjects and trauma patients. Our bench studies proved that PPLL output correlated highly with changes in path length across a model cranium. Cadaveric studies demonstrated excellent correlation between invasive and noninvasive measures of ICP using an input arterial pulse. A compact, noninvasive device for monitoring changes in intracranial distance may aid in the early detection of elevated ICP, decreasing risk of secondary brain injury and infection, and returning head-injured patients to duty.

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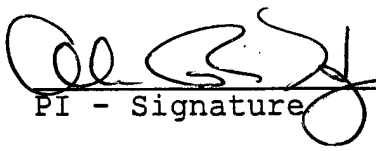

PI - Signature 2/23/98 Date

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INTRODUCTION

During this past year we accomplished all of the goals which we set forth for Year -01 on this project. First, we modified the PPLL hardware by integrating software modifications such that our clinical studies will be greatly facilitated. Although mean ICP is commonly used for ICP monitoring, the analysis of ICP waveforms is also important because the waveforms contain information on intracranial compliance and cerebrovascular tonus which cannot be estimated from mean ICP (1). Our technique, the principle of which is called pulsed phase-locked loop (PPLL), is based upon detecting skull movements which occur with fluctuations in ICP. Although the skull is often assumed to be a rigid container with a constant volume, many researchers (2-6) have demonstrated that the skull moves on the order of a few μm in association with changes in ICP. This year's studies were designed to validate our noninvasive technique for the measurement of ICP waveforms.

METHODS

The ultrasound technique we utilized to detect skull pulsation is based upon a modification of the pulsed phase-lock loop design (7), making it possible to measure slight changes in distance between an ultrasound transducer and a reflecting target. Sensitivity of the device is on the order of 0.1 μm. In the typical operation of the PPLL, the instrument transmits a 500 kHz ultrasonic tone burst through the cranium via a transducer placed on the head. The ultrasonic wave passes through the cranial cavity, reflects off the inner surface of the opposite side of the skull, and is received by the same transducer. The instrument compares the phase of emitted and received waves and alters the frequency of the next stimulus to maintain a 90° phase difference between the output of the device and the received signal. This repetition takes place at intervals of approximately 0.5 msec to 20 ms.

The details of PPLL are described elsewhere (7, 8). Briefly, if path length is changed by Δl, the frequency shift (Δf) of the ultrasound which is made to maintain the 90° phase difference between the output of the device and the received signal can be expressed as $\Delta l/l = -\Delta f/f$ (see Appendix). This is the fundamental PPLL technique. In order to provide continuous monitoring, we modified the PPLL circuit to integrate error signals of the phase shift from normal 90° phase difference (PPLL output). Theoretically, integration of the error signals also correlates with altered path length (Δl).

BENCH TESTS: A specially constructed aluminum cylinder was used to examine the PPLL output characteristics. Two pressure-resistant tubes were connected to the cylinder filled with saline. The other ends of the two tubes were connected to a plastic syringe and a fiber-optic, transducer-tipped catheter (Camino Laboratories, San Diego) which measures fluid pressure, respectively. An ultrasonic transducer was placed on the top of the cylinder. Pressure pulsations were generated at a frequency of 1 Hz by pumping the syringe while its amplitudes were changed randomly. Changes in distance were calculated from changes in ultrasound frequency.

Our model experiments demonstrated that changes in the PPLL output correlated with changes in the distance to a high degree (Fig. 1). Theoretically, the distance calculated from the ultrasound frequency can be obtained independently of PPLL output. In the results, PPLL output is expressed as:

$$\Delta\text{int (voltage)} = 2.33 \cdot 10^{-4}\ \Delta l\ (\mu\text{m}) \qquad \text{equation 1}$$

where Δint and Δl are the changes in PPLL outputs and distance, respectively.

CADAVER STUDY: Our second goal for Year-01 was to evaluate the correlation of PPLL output and directly-measured ICP in fresh human cadavera. In supine position, a catheter was inserted into the frontal horn of the right lateral ventricle through a burr hole, and the other end of the catheter was connected to pressure tubing and a plastic syringe. To correlate the PPLL output with ICP directly, a fiber-optic, transducer-tipped catheter was placed in the epidural space through another burr hole. The ultrasound transducer was placed on the temporal area above the ear and fixed with pressure cuff around the head to adjust the surface pressure on the transducer. Pulsatile changes in ICP were generated by infusing saline into the lateral ventricle at a frequency of 1 Hz. In the first experiment (cadaver A), we recorded the PPLL output while generating ICP pulsations and thereafter increased the circumference pressure around the head in steps of 10 mmHg (0-40 mmHg) by inflating the pressure cuff. In the second experiment (cadaver B), we recorded the pulsatile PPLL output by infusing saline of different temperatures into the ventricle (4°C and 20°C). The amplitudes were calculated based upon the fundamental harmonic of the data using 256 point-fast Fourier transformation (sampling rate: 50 Hz) to avoid distortion caused by other frequency waves.

RESULTS

The PPLL output closely followed the pulsatile component of ICP (Fig. 2). The results of fast Fourier transformation are provided in the top insert, showing the coincidence between the PPLL output and ICP pulse cycles. In the results of the first experiment, the ratio of PPLL amplitude to ICP amplitude significantly decreased along with increased external compression around the head:

$$y = -1.0 \cdot 10^{-5}\, x + 0.0008,\ R^2 = 0.87\ (p = 0.020)$$

where x = circumferential compression (mmHg) and y = ratio of PPLL amplitude to ICP amplitude (voltage / mmHg). In the second experiment, the correlation between the PPLL and ICP amplitudes was expressed as the same equation in both saline temperatures:

$$y = 3.0 \cdot 10^{-4}\, x + 0.0011 \qquad \text{equation 2}$$

where x = ICP amplitude (mmHg) and y = PPLL amplitude (voltage).

DISCUSSION

The results demonstrate that our PPLL device can clearly detect changes in the integrated phase shifts of the transmitted ultrasound (PPLL outputs) in association with alterations in ICP. As shown in the Appendix, the observed phase shift can be caused by changes in the distance between the transducer and the opposite side of the skull and also by changes in the ultrasound velocity in the cranium. However, we believe that changes in the PPLL output observed in our cadaveric studies represent small but detectable skull movements associated with alterations in ICP.

Infusion of saline into the ventricle could change the temperature inside the cranium, resulting in altered sound velocity. As another possible factor, changes in the density of the brain tissue due to altered ICP could affect ultrasound velocity. In the cadaver study, however, no significant difference was observed in the amplitudes of PPLL when different temperature saline was infused into the ventricle. Also, increased circumferential pressure around the head decreased PPLL amplitudes. This observation cannot be explained by changes in ultrasound velocity. This study may be the first report to measure skull movements noninvasively in association with alterations in ICP.

According to the equation 2, the ratio of PPLL amplitude to ICP amplitude is expressed as:

$$\Delta int / \Delta ICP = 3.0 \cdot 10^{-4} \text{ (voltage / mmHg)} \qquad \text{equation 3}$$

Using equations 1 (shown in the Results) and 3, the skull elastance, defined as $\Delta ICP / \Delta l$, is approximately 1.6 mmHg / μm ($=2.33 \cdot 10^{-4} / (3.0 \cdot 10^{-4}) \cdot 2$). Heisey and Adams (3) demonstrated that skull elastance in adult cats is 4.5 mmHg / μm by invasively measuring the skull movement across the sagittal suture with strain gauge. The difference between our data and theirs might be due to the difference in skull elastance between cat and human. Also, we measured skull movements transversely, while they measured the movement only across the sagittal suture. This difference in the site of measurement may affect changes in the distance obtained.

CONCLUSION

In conclusion, our technique allows analysis of ICP waveforms noninvasively and will be helpful for understanding intracranial compliance and cerebrovascular tonus in general clinical settings.

Finally we received approvals for our clinical study protocols from the IRBs at US Army, NASA Ames Research Center, and Stanford University. Similar protocols are under review now at UCSD where most future studies will be undertaken.

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8. Yost W, Cantrell J, Kushnick P (1993) Constant frequency pulsed phase-lock loop measuring device. US Patent No. 5,214,955.

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1. Ueno T, RE Ballard, LM Shuer, JH Cantrell, WT Yost, AR Hargens. Noninvasive measurement of pulsatile intracranial pressures using ultrasound Acta Neurochirurgica (in press), 1997.

2. Ueno T, RE Ballard, WT Yost, and AR Hargens. Non-invasive measurement of intracranial pressure pulsation using ultrasound. Aviation, Space and Environmental Medicine 68:(7) 646(193), 1997.

3. Ueno T, RE Ballard, LM Shuer, JH Cantrell, WT Yost, and AR Hargens. Non-invasive measurement of pulsatile intracranial pressures using ultrasound. Tenth International Symposium on Intracranial Pressure and Neuromonitoring in Brain Injury, Williamsburg, VA, 25-29 May 1997.

LIST OF PERSONNEL WHOSE SALARY IS SUPPORTED BY THIS EFFORT:

Richard E. Ballard, M.S.
Gita Murthy, M.S.
Karen Hutchinson, A.A.

FIGURE LEGENDS

Figure 1. The relation of the PPLL output to the pressure inside the cylinder and the distance between the transducer and the bottom of the tank is shown, where x = distance (μm) and y = PPLL output (voltage))

Figure 2. Typical waveforms in the PPLL output and directly measured ICP are shown as solid and dash lines, respectively. The results of frequency analysis (fast Fourier transformation) are provided in the top insert.

Figure 1

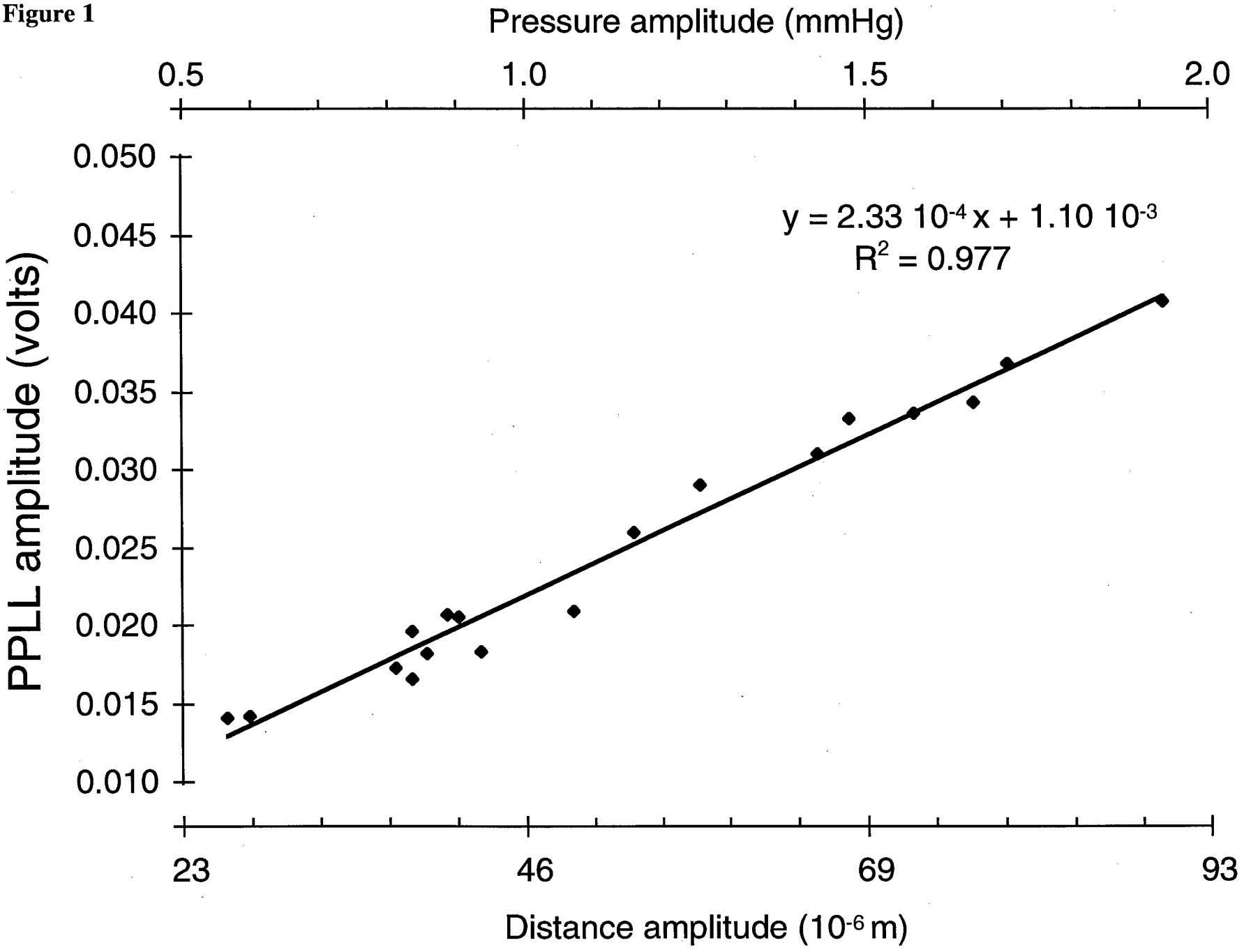
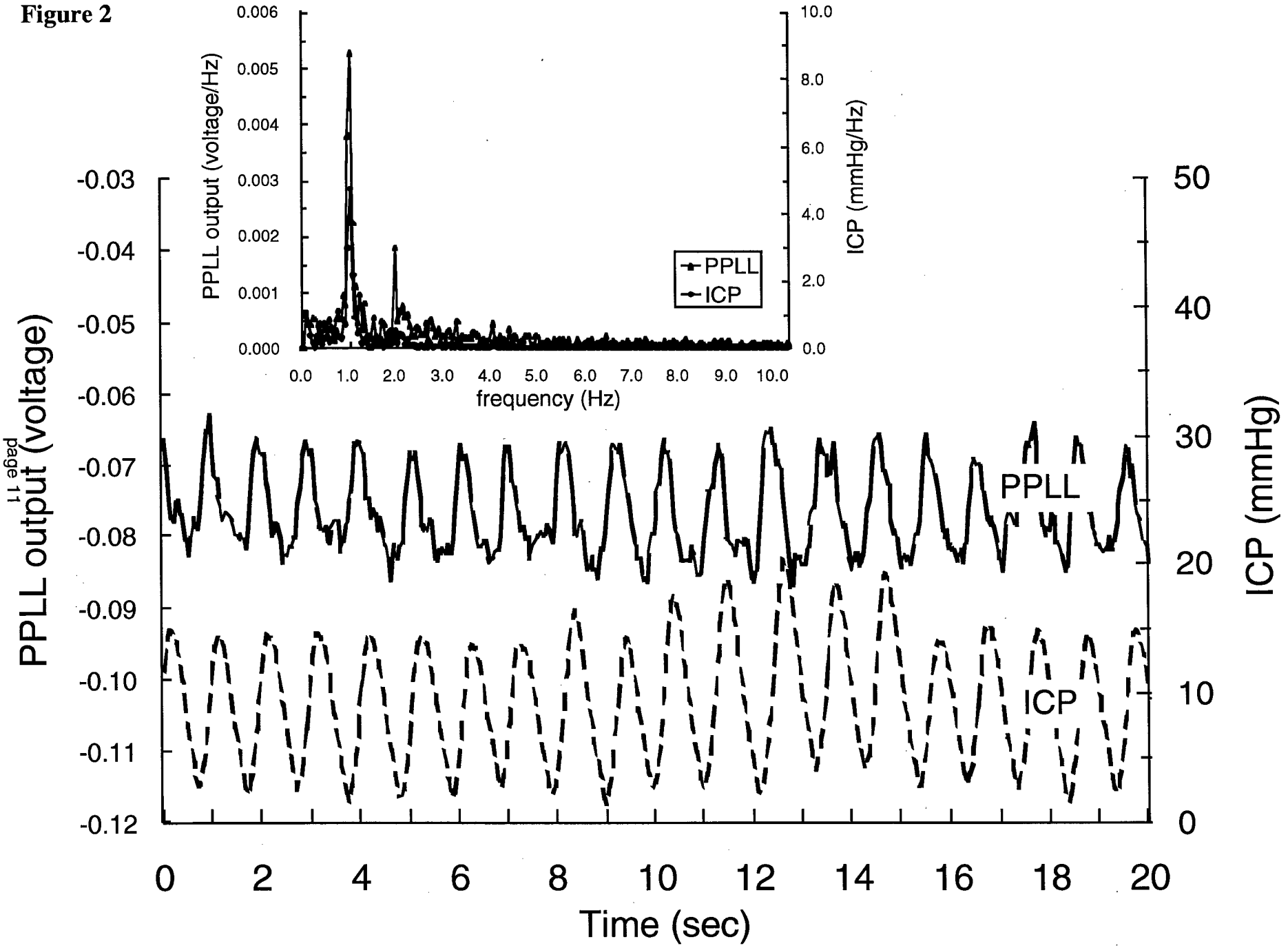

Pressure amplitude (mmHg)
0.5
1.0
1.5
2.0
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
PPLL amplitude (volts)
y = 2.33 10-4 x + 1.10 10-3
R2 = 0.977
23
46
69
93
Distance amplitude (10-6 m)

Figure 2


PPLL output (voltage/Hz)
ICP (mmHg/Hz)
frequency (Hz)
PPLL
ICP
PPLL output (voltage)
ICP (mmHg)
Time (sec)

APPENDIX

Changes in wavelength after the frequency shift which maintains a 90° phase difference between the output of the device and the received signal can be expressed as:

$$n\Delta\lambda = \Delta l \quad (\Delta\lambda\text{: changes in wavelength, } \Delta l\text{: changes in distance})$$

where $n = l/\lambda$ (l: initial distance between a transducer and a target, λ: initial wavelength).

Therefore, $$\frac{\Delta\lambda}{\lambda} = \frac{\Delta l}{l}$$

Also, $\Delta\lambda = \frac{\partial\lambda}{\partial v}\Delta v + \frac{\partial\lambda}{\partial f}\Delta f$ where Δv is changes in ultrasound velocity. and $f = v/\lambda$.

Solving these equations, we obtain $$\frac{\Delta f}{f} = \frac{\Delta v}{v} - \frac{\Delta l}{l}$$

If changes in sound velocity are negligible, the above equation is finally expressed as:

$$\frac{\Delta f}{f} = -\frac{\Delta l}{l}$$

Acta Neurochirurgica, 1997 (in press)

May 20, 1997

1 title page
6 text pages
9 references
2 figures

Noninvasive Measurement of Pulsatile Intracranial Pressure using Ultrasound

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[1]Gravitational Research Branch (239-11), NASA Ames Research Center

[2]Department of Neurosurgery, Stanford University Medical Center

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NASA Ames Research Center

Moffett Field, CA 94035-1000

SUMMARY

The present study was designed to validate our noninvasive ultrasonic technique (pulse phase locked loop: PPLL) for measuring intracranial pressure (ICP) waveforms. The technique is based upon detecting skull movements which are known to occur in conjunction with altered intracranial pressure. In bench model studies, PPLL output was highly correlated with changes in the distance between a transducer and a reflecting target (R^2=0.977). In cadaver studies, transcranial distance was measured while pulsations of ICP (amplitudes of zero to 10 mmHg) were generated by rhythmic injections of saline. Frequency analyses (fast Fourier transformation) clearly demonstrate the correspondence between the PPLL output and ICP pulse cycles. Although theoretically there is a slight possibility that changes in the PPLL output are caused by changes in the ultrasonic velocity of brain tissue, the decreased amplitudes of the PPLL output as the external compression of the head was increased indicates that the PPLL output represents substantial skull movement associated with altered ICP. In conclusion, the ultrasound device has sufficient sensitivity to detect transcranial pulsations which occur in association with the cardiac cycle. Our technique makes it possible to analyze ICP waveforms noninvasively and will be helpful for understanding intracranial compliance and cerebrovascular circulation. (200 words)

INTRODUCTION

Elevated intracranial pressure (ICP) is used as a sign of neurological deterioration in the management of patients with head trauma, cerebrovascular diseases, and brain tumors (6). Conventional methods for ICP monitoring require surgical procedures which are accompanied by increased risk of infection. For this reason, candidates for ICP monitoring are currently only patients with severe neurological conditions. A noninvasive technique could make it possible to monitor ICP more easily and repeatedly in patients with a variety of neurosurgical conditions, thus aiding clinical management and reducing the mortality and morbidity related to neurological diseases.

We have developed a new ultrasonic device to measure ICP waveforms. Although mean ICP is commonly used for ICP monitoring, the analysis of ICP waveforms is also important because the waveforms contain information on intracranial compliance and cerebrovascular tonus, which cannot be estimated from mean ICP (1). Our technique (8), the principle of which is called pulsed phase-locked loop

(PPLL) method, is based upon detecting skull movements which occur with fluctuations in ICP. Although the skull is often assumed to be a rigid container with a constant volume, many researchers (2-5, 7) have demonstrated that the skull moves on the order of a few μm in association with changes in ICP. The present study was designed to validate our noninvasive technique for the measurement of ICP waveforms.

TECHNIQUE

The ultrasound technique (8) we utilized to detect skull pulsation is based upon a modification of the pulsed phase-lock loop design, which makes it possible to measure slight changes in distance between an ultrasound transducer and a reflecting target. Sensitivity of the device is on the order of 0.1 μm. In the typical operation of the PPLL, the instrument transmits a 500 kHz ultrasonic tone burst through the cranium via a transducer placed on the head. The ultrasonic wave passes through the cranial cavity, reflects off the inner surface of the opposite side of the skull, and is received by the same transducer. The instrument compares the phase of emitted and received waves and alters the frequency of the next stimulus to maintain a 90° phase difference between the output of the device and the received signal. This repetition takes place at intervals of approximately 0.5 msec to 20 ms.

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BENCH TEST: A specially constructed aluminum cylinder was used to examine the PPLL output characteristics. Two pressure-resistant tubes were connected to the cylinder filled with saline. The other ends of the two tubes were connected to a plastic syringe and a fiber-optic, transducer-tipped catheter (Camino Laboratories, San Diego) which measures fluid pressure, respectively. An ultrasonic transducer

was placed on the top of the cylinder. Pressure pulsations were generated at a frequency of 1 Hz by pumping the syringe while its amplitudes were changed randomly. Changes in distance were calculated from changes in ultrasound frequency.

CADAVER STUDY: The correlation between the PPLL output and ICP were evaluated in two fresh cadavera (age 85 and 90) which were less than 48 hours postmortem. In supine position, a catheter was inserted to the frontal horn of the right lateral ventricle through a burr hole, and the other end of the catheter was connected to pressure tubing and a plastic syringe. To correlate the PPLL output with ICP directly, a fiber-optic, transducer-tipped catheter was placed in the epidural space through another burr hole. The ultrasound transducer was placed on the temporal area above the ear and fixed with pressure cuff around the head to adjust the surface pressure on the transducer. Pulsatile changes in ICP were generated by infusing saline into the lateral ventricle at a frequency of 1 Hz. In the first experiment (cadaver A), we recorded the PPLL output while generating ICP pulsations and thereafter increased the circumference pressure around the head in steps of 10 mmHg (0-40 mmHg) by inflating the pressure cuff. In the second experiment (cadaver B), we recorded the pulsatile PPLL output by infusing saline of different temperatures into the ventricle (4°C and 20°C).

DATA ANALYSIS: The amplitudes were calculated based upon the fundamental harmonic of the data using 256 point-fast Fourier transformation (sampling rate: 50 Hz) to avoid distortion caused by other frequency waves.

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$$y = 3.0 \cdot 10^{-4} x + 0.0011 \qquad \text{equation 2}$$

where x = ICP amplitude (mmHg) and y = PPLL amplitude (voltage).

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The results demonstrate that our PPLL device can clearly detect changes in the integrated phase shifts of the transmitted ultrasound (PPLL outputs) in association with alterations in ICP. As shown in the Appendix, the observed phase shift can be caused by changes in the distance between the transducer and the opposite side of the skull and also by changes in the ultrasound velocity in the cranium. However, we believe that changes in the PPLL output observed in the present cadaveric study represent small but detectable skull movements associated with alterations in ICP.

Infusion of saline into the ventricle could change the temperature inside the cranium, resulting in altered sound velocity. As another possible factor, changes in the density of the brain tissue due to altered ICP could affect ultrasound velocity. In the cadaver study, however, no significant difference was observed in the amplitudes of PPLL when different temperature saline was infused into the ventricle. Also, increased circumference pressure around the head decreased PPLL amplitudes. This observation cannot be explained by changes in ultrasound velocity. This study may be the first report to measure skull movements noninvasively in association with alterations in ICP.

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ACKNOWLEDGEMENTS

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$n\Delta\lambda = \Delta l$ ($\Delta\lambda$: changes in wavelength, Δl: changes in distance)

where $n = l/\lambda$ (l: initial distance between a transducer and a target, λ: initial wavelength).

Therefore, $\frac{\Delta\lambda}{\lambda} = \frac{\Delta l}{l}$

Also, $\Delta\lambda = \frac{\partial\lambda}{\partial v}\Delta v + \frac{\partial\lambda}{\partial f}\Delta f$ where Δv is changes in ultrasound velocity. and $f = v/\lambda$.

Solving these equations, we obtain $\frac{\Delta f}{f} = \frac{\Delta v}{v} - \frac{\Delta l}{l}$

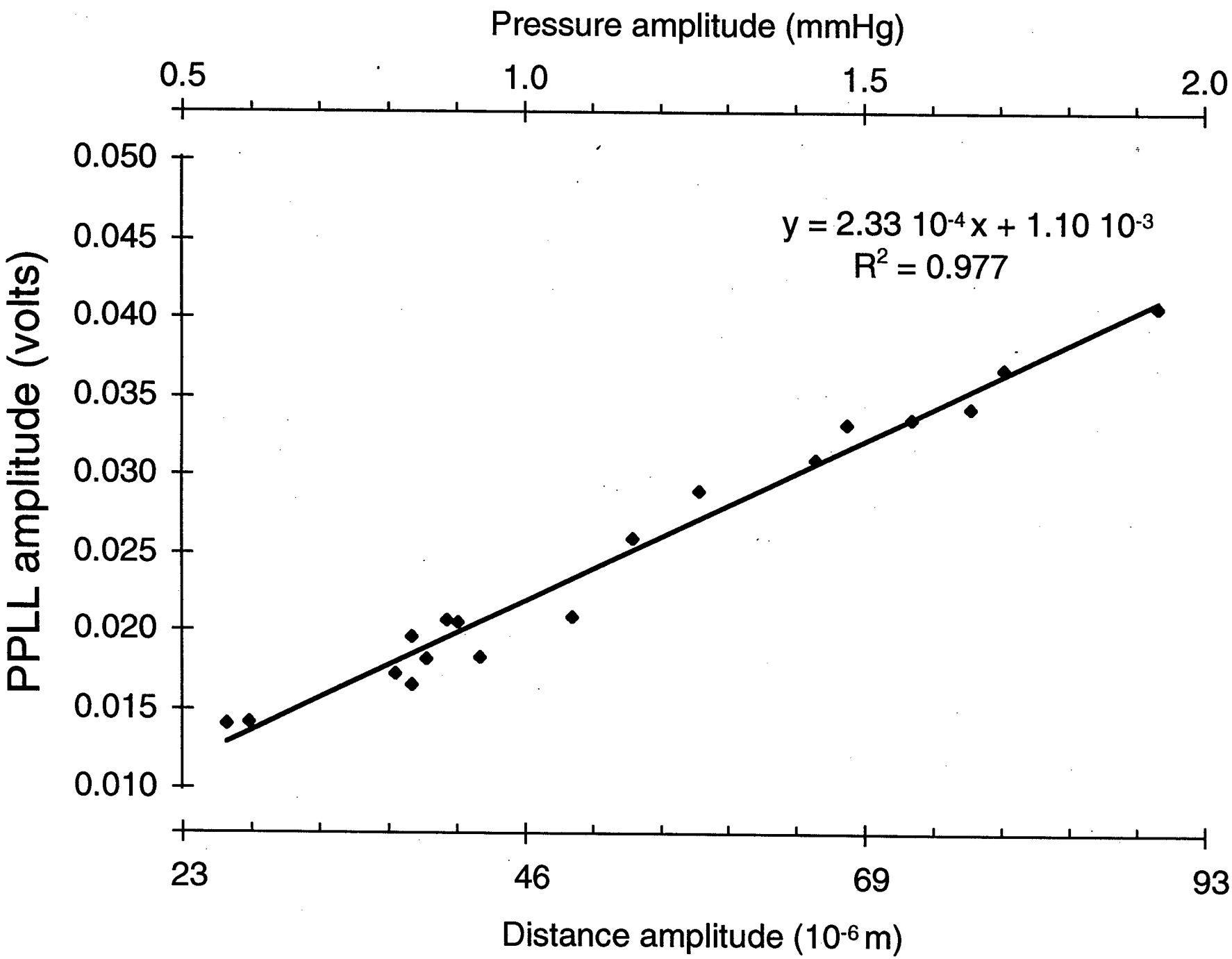
If changes in sound velocity are negligible, the above equation is finally expressed as

$$\frac{\Delta f}{f} = -\frac{\Delta l}{l}$$

FIGURE LEGEND

Figure 1. The relation of the PPLL output to the pressure inside the cylinder and the distance between the transducer and the bottom of the tank is shown, where x = distance (μm) and y = PPLL output (voltage))

Figure 2. Typical waveforms in the PPLL output and directly measured ICP are shown as solid and dash lines, respectively. The results of frequency analysis (fast Fourier transformation) are provided in the top insert.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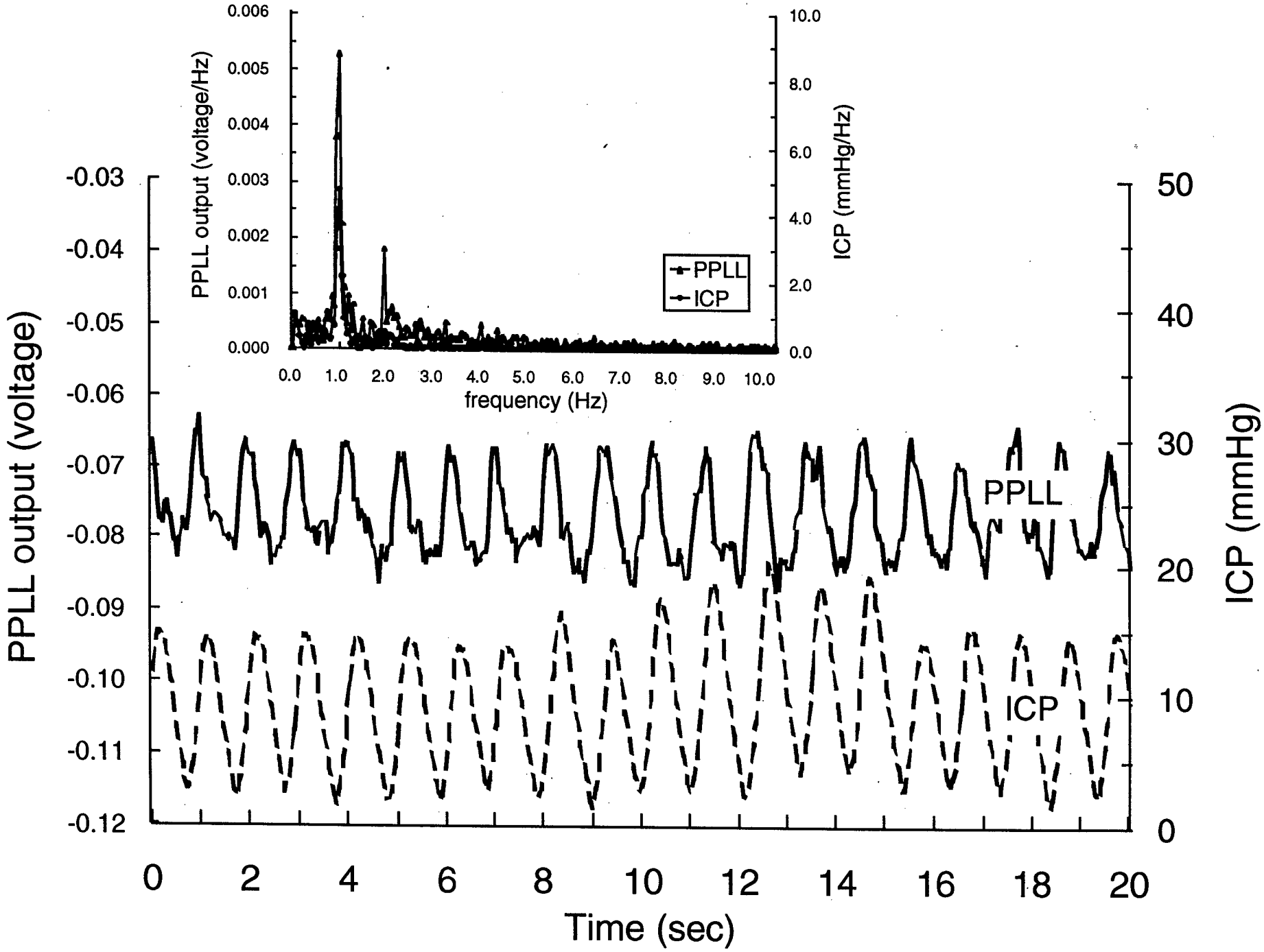
1.0
1.5
2.0
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
PPLL amplitude (volts)
y = 2.33 10-4 x + 1.10 10-3
R2 = 0.977
23
46
69
93
Distance amplitude (10-6 m)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ICP (mmHg)
Time (sec)
PPLL
ICP
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-0.08
-0.09
-0.10
-0.11
-0.12
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10
0
0
2
4
6
8
10
12
14
16
18
20
PPLL output (voltage/Hz)
ICP (mmHg/Hz)
frequency (Hz)
PPLL
ICP
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0.004
0.003
0.002
0.001
0.000
10.0
8.0
6.0
4.0
2.0
0.0
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0

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STRING ANALYSIS OF INSTRUMENT SCAN PATTERNS RECORDED WHILE FLYING A MOTION-BASED HELICOPTER TRAINING SIMULATOR. L.A. Temme*, J. Woodall, and D. L. Still. Naval Aerospace Medical Research Laboratory, Pensacola, FL 32508-1046

INTRODUCTION: Last year we reported the amount of time Navy helo pilots viewed each flight instrument as they executed instrument flight maneuvers in a motion-based helo simulator fitted with a noninvasive eye tracker. These data were presented as Dwell Times (DT), the amount of time a pilot's line-of-sight (los) was directed to each instrument. DT provides no information about the sequence of instruments viewed. For that we need to know what instrument was being viewed or fixated upon at a particular time, fixations being a finer level of analysis than DT. The eye-tracker raw data (los measured at 60-Hz) are at too fine a level, reporting eye pointing at the instant of measurement. The problem is noise. Eyes make a variety of movements, even when they are fixating on something. The question is: How do you define a fixation from the 60-Hz los data? or equivalently: How much movement does the eye make before it is fixating elsewhere? Like many good problems, this one has been around for a while so standard averaging algorithms are available to convert los data to fixations. The algorithms require specifying parameters that define spatiotemporal averaging, but beg the issue of the resultant fixations' dependence upon the parameter values. How do we pick good values? METHODS: We used String Analysis (SA) to calculate the similarity ,S, between scans. SA, a technique that has only recently been applied to eye movement research, calculates the similarity between pairs of strings. We input the same los raw data to a fixation algorithm with ranges of parameters, generating families of fixation strings whose Ss were calculated. RESULTS: The lawfulness of the fixation Ss upon the parameters provided parameter boundary values. CONCLUSIONS: SA defined a range of reasonable parameter values; but more importantly, SA promises to be a valuable tool for visual scan research.

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ARTERIALIZED EAR LOBE SAMPLES FOR ARTERIAL BLOOD GAS TENSIONS WITH AND WITHOUT HYPOXIA DURING 6° HEAD-DOWN TILT

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Introduction: The need to measure accurately the partial pressures of O_2 and CO_2 in arterial blood has increased with plans for long duration manned space missions, especially in emergency scenarios (hypoxia). The arterialized ear lobe technique for blood gas tensions, as a substitute for arterial cannulation and punctures, has been used in clinical medicine for more than 30 years, but has not been examined during space missions and ground-based microgravity simulations. Pre-Study: In order to evaluate the effects of head congestion on this technique, the end-tidal-arterialized differences of PO_2 (ET-ac PO_2) and PCO_2 (ET-ac PCO_2) were investigated. Seven subjects laid supine with and without an inflated cuff (10 mm Hg) around the neck, which produced head congestion without the cardiopulmonary changes associated with 6° HDT. The mean ET-ac PO_2 and PCO_2 differences were 7.4, 7.5, 7.7 mm Hg and 0.5, 0.6, 0.6 mm Hg, respectively, during baseline, cuff inflation and recovery ($p>0.05$). Methods: The ET-ac PO_2 and PCO_2 were measured in six subjects at the end of 30 minute supine (baseline) and 6° HDT posture during normoxia and hypoxia (inspired O_2 of 10.7%). The ear lobe was arterialized by means of a 5 minute massage with a vasodilating cream and a small incision was made in the ear lobe with a sterile surgical blade for blood sample collection. The arterialized capillary PO_2 and PCO_2 were compared with simultaneous end-tidal PO_2 and PCO_2 measurements to determine the ET-ac differences in each posture during normoxia and hypoxia. Results: The mean ET-ac PO_2 differences were 8.9, 10.2 mm Hg in normoxia and 4.7, 3.8 mm Hg in hypoxia during supine and 6° HDT, respectively ($p>0.05$). The mean ET-ac PCO_2 differences were 0.8, 0.1 in normoxia and 2.0, 1.4 in hypoxia during supine and 6° HDT, respectively ($p>0.05$). Conclusion: The ground-based microgravity simulation (6° HDT) used in this study did not alter the end-tidal-arterialized capillary PO_2 or PCO_2 differences from control values. Studies should be conducted during parabolic flights and/or space missions in order to improve the technique with regard to blood handling and restraint of the astronaut in microgravity.

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NON-INVASIVE MEASUREMENT OF INTRACRANIAL PRESSURE PULSATION USING ULTRASOUND

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INTRODUCTION Exposure to microgravity causes a cephalad fluid shift which may elevate intracranial pressure (ICP). Elevation in ICP may affect cerebral hemodynamics in astronauts during space flight. ICP is, however, a difficult parameter to measure due to the invasiveness of currently available techniques. We already reported our development of a non-invasive ultrasound device for measurement of ICP. We recently modified the device so that we might reproducibly estimate ICP changes in association with cardiac cycles. **METHODS** In the first experiment, we measured changes in cranial distance with the ultrasound device in cadavera while changing ICP by infusing saline into the lateral ventricle. In the second experiment, we measured changes in cranial distance in five healthy volunteers while placing them in 60°, 30° head-up tilt, supine, and 10° head-down tilt position. **RESULTS** In the cadaver study, fast Fourier transformation revealed that cranial pulsation is clearly associated with ICP pulsation. The ratio of cranial distance and ICP pulsation is 1.3μm/mmHg. In the tilting study, the magnitudes of cranial pulsation are linearly correlated to tilt angles ($r=0.87$). **CONCLUSION** The ultrasound device has sufficient sensitivity to detect cranial pulsation in association with cardiac cycles. By analyzing the magnitude of cranial pulsation, estimates of ICP during space flight are possible. (Supported by NASA grant 199-26-12-34)

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RECENT SUCCESSFUL CARDIOVASCULAR COUNTERMEASURES FOR SPACE FLIGHT

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Two related cardiovascular concerns led to the development of countermeasures which decreased risk for flight crew subjects. In the first case, the mandatory, multilayered protective garment worn during launch and entry (Launch and Entry Suit or LES) imposes a metabolic and thermal load on crewmen. This metabolic load was manifested as decreased orthostatic tolerance in astronaut participants of post relative to pre- Challenger missions. An approximate doubling of orthostatic intolerance was observed in the post Challenger group. Since return to flight following the Challenger accident, crewmen have worn a LES which was cooled only by a fan assembly that ducted cabin air into the garment across the thoracic area. Attempts to enhance the air cooling mode proved unsuccessful. Addition of a full torso liquid cooling garment to the LES ensemble resulted in a satisfactory countermeasure. Laboratory simulation and flight results documenting this approach will be discussed. The second cardiovascular issue which required development of a countermeasure related to potential deconditioning associated with long term space flight followed by exposure to significant +Gz during seated reentry in the Shuttle. Shuttle experience with orthostatic intolerance at landing raised safety concerns regarding astronauts and cosmonauts returning from missions of 4-6 months on Mir. Soyuz vehicles return their cosmonauts supine with the acceleration load +Gx (front to back). If a crewman became orthostatically intolerant during seated reentry on the Shuttle, there would be an approximate 15 m period when no assistance could be rendered, with the potential for cerebral damage. A conservative programmatic decision was made to return long duration crews in the supine posture until sufficient experience had been gained to assess the risk of seated reentry. The Flight Crew Support Division in consultation with the Medical Sciences Division designed, manufactured, and provided the Recumbent Seating System (RSS) for use on Shuttle. This system accommodates up to three crewmen on the Shuttle mid deck floor. Its successful use for return of the Mir 18 crew on STS 71 will be discussed.

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INCREASED BARORECEPTOR SENSITIVITY IS ASSOCIATED WITH INCREASED SUSCEPTIBILITY TO CORIOLIS STRESS. JC Finley, MJ O'Leary, MR Maasdam, *SL Farrow, BD Lawenda, DC Wester, and WE Lockette. Naval Medical Center, San Diego, CA; University of Michigan Medical School, Ann Arbor; and Veterans Administration Medical Center, Detroit, MI.

We reported that a genetic polymorphism of the alpha-2 adrenergic receptor is associated with a heritable susceptibility to motion sickness and orthostatic intolerance. We tested our hypothesis that given a common genetic basis for these phenotypes, subjects with increased susceptibility to motion sickness should have orthostatic intolerance. Coriolis stress susceptibility (CSS) was measured by determining the number of off-axis head movements a subject could complete while being rotated at increasing velocity before they developed motion sickness, and cardiovascular responses to graded lower body negative pressure (LBNP) were recorded using digital impedance cardiography. When stratified by CSS scores, subjects with either very high (≤200 head movements, n=8) or very low (≥300 head movements, n=12) sensitivity to motion sickness induction (values in percent change from baseline ± SEM) had no differences in heart rate (15 ± 5 vs. 11 ± 3, respectively), systemic vascular resistance (25 ± 9 vs. 47 ± 10), or systolic blood pressure (8 ± 3 vs. 4 ± 2) responses induced with -40mmHg LBNP. In many subjects, baroreceptor function could not be determined at higher levels of LBNP due to the development of presyncopal symptoms at -40 and -60 mmHg (44% of subjects tested, n=18); furthermore, presyncopal symptoms developed in 86% of subjects with increased susceptibility to CSS in comparison to only 18% in subjects who demonstrated low sensitivity to CSS ($X^2 = 8.03$, $df = 1$, $p = .005$). Despite a common heritable basis for susceptibility to Coriolis and orthostatic stress, epistatic factors may modify the phenotypic expression of these traits; however, Coriolis stress susceptibility is associated with intolerance to high, but not low, degrees of orthostatic stress.

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CEREBROVASCULAR RESPONSES DURING LOWER BODY NEGATIVE PRESSURE-INDUCED PRESYNCOPE. K. Kuriyama, T. Ueno*, R.E. Ballard*, D.E. Watenpaugh, S.M. Fortney, and A.R. Hargens*. Gravitational Research Branch (239-11), NASA Ames Research Center, Moffett Field, CA 94035.

INTRODUCTION. Reduced orthostatic tolerance is commonly observed after space flight, occasionally causing presyncopal conditions. Although the cerebrovascular system may play an important role in presyncope, there have been few reports concerning cerebral hemodynamics during presyncope. The purpose of this study was to investigate cerebrovascular responses during presyncope induced by lower body negative pressure (LBNP). METHODS. Seven healthy male volunteers were exposed to LBNP in steps of -10 mmHg every 3 min until presyncopal symptoms were detected. Blood pressure (BP) and heart rate (HR) were measured with a finger cuff. Cerebral tissue oxy- and deoxy- hemoglobin (Hb) concentrations were estimated using near infrared spectroscopy (NIRS). Cerebral blood flow (CBF) velocity at the middle cerebral artery was measured with transcranial Doppler sonography (TCD). We focused on the data during the 2 min before endpoint. RESULTS. BP marked a gradual decrease (91 to 86 mmHg from 2 min to 30 sec before endpoint), which was accelerated along with HR decrease during the final 30 sec (86 to 71 mmHg). Cerebral oxy-Hb concentration decreases as presyncope is approached while total-Hb concentration remains fairly constant. TCD reveals a decrease in the CBF velocity. The TCD and NIRS results suggest that CBF decreases along with the BP decrease. CONCLUSION. Cerebrovascular responses during presyncope are closely related to cardiovascular responses. (Supported by NASA grant 199-26-12-34).

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NON-INVASIVE MEASUREMENT OF PULSATILE INTRACRANIAL PRESSURES USING ULTRASOUND

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Introduction Early detection of elevated intracranial pressure (ICP) will aid clinical decision-making for head trauma, brain tumor and other cerebrovascular diseases. Conventional methods, however, require surgical procedures which take time and are accompanied by increased risk of infection. Accordingly, we have developed and refined a new ultrasound device [1] to measure skull movement which are known to occur in conjunction with altered ICP [2]. The principle of this device is based upon pulse phase locked loop (PPLL), which enables us to detect changes in distance on the order of μm between an ultrasound transducer on one side of the skull and the opposite inner surface of the cranium. The present study was designed to verify this measurement technique in cadavera.

Methods Transcranial distance was increased in steps of 10 mmHg from zero to 50 mmHg by saline infusion into the lateral ventricle of two cadavera. In separate experiments, pulsations of ICP with the amplitudes of zero to 2 mmHg were generated by rhythmic injections of saline using a syringe.

Results When the ICP was stepwise increased from zero to 50 mmHg, transcranial distance increased in proportion with the ICP increase ($y=12x-76$, $r=0.938$), where y is changes in transcranial distance in μm and x is ICP in mmHg. In the data recorded while ICP pulsations were generated, fast Fourier transform analysis demonstrated that cranial pulsations were clearly associated with ICP pulsations.

Summary and Conclusions The results indicate that changes in transcranial distance is linearly correlated with those in ICP, and also that the PPLL device has sufficient sensitivity to detect transcranial pulsations which occur in association with the cardiac cycle. By analyzing the magnitude of cranial pulsations, we may be able to estimate the pressure-volume index in the cranium. As a result, estimates of intracranial compliance may be possible by using the PPLL device. Further studies are necessary in normal subjects and patients. (Supported by NASA and the US Amy Medical Research Material Command, and a National Research Council senior fellowship to TU)

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